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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,665	11/12/2003	Akira Nishiyama	21581-00240-US1	5354
30678	7590	03/19/2004	EXAMINER	
CONNOLLY BOVE LODGE & HUTZ LLP SUITE 800 1990 M STREET NW WASHINGTON, DC 20036-3425			ZUCKER, PAUL A	
			ART UNIT	PAPER NUMBER
			1621	

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/705,665

Applicant(s)

NISHIYAMA ET AL.

Examiner

Paul A. Zucker

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-18 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 5-18 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 09/762,215.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 11/12/2003.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Specification

1. The abstract of the disclosure is objected to because it consists of more than a single paragraph. Applicants should amend the abstract so that it consists of a single paragraph. Correction is required. See MPEP § 608.01(b).

Improper Amendment

2. According to § 1.173 the specification of the reissue application must include the entire specification and claims of the patent, with the matter to be omitted by reissue enclosed in square brackets; and any additions made by the reissue must be underlined, so that the old and the new specifications and claims may be readily compared. In the instant case the limitations deleted from claim 1 have not been set forth in square brackets. Applicants are required to submit an amendment to claim 1 that is proper under § 1.173.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-3, 5 and 14-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is drawn to a process for producing a 5-hydroxy-3-oxopentanoic acid derivative of the formula (IV), but, since the claim does not set forth any steps involved in the method/process, it is unclear

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what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a process without any active, positive steps delimiting how this process is actually practiced. Claim 1 and its dependents are therefore rendered indefinite.

4. Claims 1-3, 5 and 14-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the limitation "R³" in lines 12 and 15. There is, however, no R³ in the structure set forth. Claim 1 and its dependents are therefore rendered indefinite.
5. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 17 recites the limitation "compound (II) or (VI)" in line 2. There is insufficient antecedent basis for this limitation in the claim.
6. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 18 recites the limitation "acetic acid ester" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wess et al (US 4,970,313 11-1990).

Instantly claimed is a process for producing a 5-hydroxy-3-oxopentanoic acid derivative of formula (IV) which comprises allowing a lithium amide of formula (III) to act upon a mixture of acetic acid ester (I) and halomagnesium alcoholate (VI).

Wess teaches (Column 9, lines 1-25) a process for producing a 5-hydroxy-3-oxopentanoic acid derivative of formula (IV) by the reaction of lithium diisopropylamide (formed *in situ*) with tert-butyl acetate and methyl S-3-hydroxy-4-(t-butyldiphenylsilyloxy) butyrate. Weiss further teaches reaction at -15°C .

The difference in the process taught by Wess and that instantly claimed is that, in the instant process, the t-butyldiphenylsilyl group in methyl S-3-hydroxy-4-(t-butyldiphenylsilyloxy) butyrate is replaced by a halo magnesium group.

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Weiss, however, suggests (Column 5, lines 49-52) that a version of the process he teaches may employ the magnesium alcoholate corresponding to the instant halomagnesium alcoholate (VI). The selection of chloride as a magnesium counterion is within the skill of the ordinary artisan.

One of ordinary skill in the art would have been motivated to make the substitution of the magnesium alcoholate for the t-butyldiphenylsilyl group in the process exemplified by Wess in order to obviate the need for the two synthetic steps of hydroxyl protection and deprotection. Because Wess suggests the suitability of the substitution, there would have been a reasonable expectation for success.

Thus the instantly claimed process would have been obvious to one of ordinary skill in the art.

8. Claim 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wess et al (US 4,970,313 11-1990) as applied to claim 10-13 above, and further in view of Solomons (Organic Chemistry, 5th Edition, 1992, John Wiley & Sons, Inc., New York, pages 461-462).

Instantly claimed is a process for producing a 5-hydroxy-3-oxopentanoic acid derivative of formula (IV) which comprises allowing a lithium amide of formula (III) to act upon a mixture of acetic acid ester (I) and halomagnesium alcoholate (VI) which is formed by the reaction of an alcohol of formula (II) and a Grignard reagent of formula (V).

The difference between the process taught by Wess and that instantly claimed is that Wess is silent regarding the method of formation of the magnesium alcoholate he suggests the use of.

Solomons, however, teaches (Page 462, top, 2nd equation) that an alcohol reacts with a Grignard reagent to yield the corresponding halomagnesium alcoholate and the corresponding hydrocarbon. The advantage of using the Grignard to form the alcoholate is that the only other by-product is an inert hydrocarbon.

One of ordinary skill in the art would have been motivated to use the Grignard reagent to form a magnesium alcoholate since only inert by-products are produced in addition to the desired alcoholate. Because simple acid-base chemistry is involved there would have been a reasonable expectation for success.

Thus the instantly claimed process would have been obvious to one of ordinary skill in the art.

Conclusion

9. Claims 1-3, and 5-18 are pending. Claims 1-3, and 5-18 are rejected.

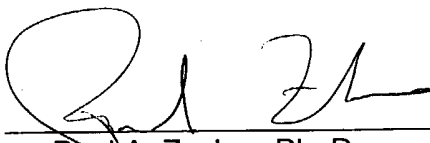
10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Brower et al (Tetrahedron Letters, The Synthesis of (4R-cis)-1,1-Dimethylethylcyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate, a Key Intermediate for the Preparation of CI-981, a High Potent, Tissue Selective Inhibitor of HMG-CoA Reductase, 1992, 33(17), pages 2279-2282). Brower teaches (Page

2280, last equation) a synthesis of a compound instant formula (IV) via a similar process without magnesium.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 571-272-0650. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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